PROPOSER INFORMATION PAMPHLET for BAA 06-31
FOR THE DEFENSE ADVANCED RESEARCH PROJECTS AGENCY (DARPA)
ACCELERATED MANUFACTURING OF PHARMACEUTICALS

This Performer Information Pamphlet is exclusively for the 42 month "Accelerated Manufacturing of Pharmaceuticals" BAA and does not apply to any other program.

1.0 Program Objective

The Defense Sciences Office (DSO) of the Defense Advanced Research Projects Agency (DARPA) is seeking proposals for new technologies that radically accelerate the manufacturing of protein vaccines and protein-based therapeutics. This program is a key component of an overall DARPA focus to accelerate the insertion of critical therapeutics essential for the military.

The vision of the Accelerated Manufacturing of Pharmaceuticals (AMP) program is to create an extremely rapid, flexible and cost-effective manufacturing system capable of producing three million doses of GMP-quality vaccines or monoclonal antibodies (mAB) within 12 weeks. The 12 week timeline commences from the point when the target antigen or genetic sequence is delivered to the manufacturer and not after a stable clone or F1 generation is developed. This revolutionary manufacturing platform will have extraordinary flexibility, allowing for the manufacture of vaccines to protect against a wide range of viral, protozoan, fungal, bacterial and bio-toxin threats. The monoclonal antibodies produced by the platform will have the same efficacy and characteristics as current FDA-approved monoclonal antibodies. Strong preference will be given to platforms that are capable of producing both small monomeric proteins (vaccine-like) and monoclonal antibodies.

All proposers to this BAA must provide evidence of a highly integrated, multi-disciplinary team capable of fulfilling the entire vision, meeting all program objectives and milestones for each phase of the program. These milestones are detailed in this Proposer Information Pamphlet and in the associated BAA. Details regarding the team composition and the responsibilities of the Program Manager/System Integrator (SI) are provided in sections 3.2 and 3.3.

At the conclusion of this program, the proposer will deliver a high capacity, rapid vaccine and/or monoclonal antibody manufacturing system ready for transition to a commercialization partner and capable of producing protein therapeutics that are eligible for FDA approval.

This effort will be conducted over three phases of 12, 15 and 15 months, respectively. Each phase requires logarithmic increases in the number of doses of vaccine and/or monoclonal antibody produced in the candidate system. Based on the results of each Phase and the availability of funding, a down-select is possible. **Successful completion of any phase does not guarantee selection in the next phase**. Each proposer applying to the Accelerating Manufacturing of Pharmaceuticals BAA must accurately and completely address the technical challenges listed in the milestones set forth for Phase I and Phase II as well as a discussion of path to accomplish the milestones in Phase III.

2.0 Background and Motivation

DARPA's vision is to create technologies that will enable the Department of Defense (DoD) to have a rapid (within weeks) and highly effective medical therapeutic response to any intentional or naturally emergent pathogen. This flexible response strategy is in sharp contrast to the current system that requires years (in some cases decades) of research, development, production, and stockpiling of medical therapeutics against anticipated pathogens. A key component of a rapid response strategy is the ability to manufacture millions of doses of potentially diverse biological therapeutics within weeks.

Current efforts to improve upon the speed, flexibility and cost-effectiveness of current vaccines and monoclonal manufacturing systems are impeded by inherent rate-limiting metabolic processes. For example, current methods of production, including next generation CHO cells for mAB production and human proteins, as well as accelerated egg-based vaccine manufacturing systems, continue to be slow and unreliable, generally taking years to optimize prior to large scale production of a new vaccine or immune therapy. Furthermore, recent problems with egg-based vaccine manufacture such as unexpected contamination, unprecedented shortages of special pathogen-free (SPF) eggs, and inability to grow certain viruses in eggs, have demonstrated additional vulnerabilities in these traditional manufacturing methods. More recent technologies such as prokaryote and yeast-based fermentation systems, although commonly regarded as faster than eggs and CHO cells, are less likely to produce therapeutic proteins that require human-like post-translational modifications. Each of the protein therapeutic and vaccine production systems currently in use are incapable of meeting the medical needs of a large scale biological disaster such as the intentional release of a contagious biological agent or to mitigate against a rapidly emerging pandemic. There are additional problems with maintaining adequate stockpiles of expensive immune therapies such as post-exposure monoclonal antibodies and animal serum-derived antitoxins. These proteins (often called "biologics") require refrigeration, have a limited shelf life, and need to be replenished at intervals of 6-24-months at considerable expense to the DoD. In addition, it is impossible to predict, develop, purchase and store monoclonal countermeasures for all possible etiologic agents that might result from natural-occurring or intentional biological threats.

One under-emphasized point in preplanning for mass casualty infections or poisonings is that the identity of a new biological threat agent is unlikely to be known in advance and therefore pre-emptive manufacturing and stockpiling of countermeasures can not be performed. Since current-generation vaccine and protein manufacturing systems require many months to years to produce, these systems may fail to provide timely, flexible and cost-effective therapies to protect against a mass-casualty infection or poisoning. Our military's operational readiness, high vulnerability and need for specific vaccines and monoclonal therapies require a radical solution to replace the current slow scale-up and manufacture of these life saving drugs.

The goal of Accelerated Manufacturing of Pharmaceuticals is to significantly shorten the time required to produce high quality protein therapeutics. The ability to produce therapeutics or vaccines "on demand," in large quantity, at low cost, and to interdict both established and new agents, would obviate the need for large national stockpiles and revolutionize our ability to definitely respond to biological threats.

3.0 Scope

AMP is an aggressive three phase, 42-month program with a goal of revolutionizing the manufacture of protein therapeutics and vaccines. Unlike previous DARPA programs, the focus of AMP is not to develop new therapeutics or vaccines, but rather to develop new technologies to speed the manufacture of protein based drugs and vaccines to meet the needs of the warfighter. As a result of high efficiency and rapid protein manufacture, AMP will also prove to be a cost-efficient and easily-scaled up system that on completion will reliably produce over 3 million doses of vaccine or protein therapeutic in 12 weeks. In is DARPA's intention that the AMP platform(s) will not lie idle between production runs to supply military vaccines and therapeutics. The plasticity, speed and cost effectiveness of the AMP system allow the technology to be supported by other drug markets such as to produce growth factors, cytokines, serum proteases, civilian or veterinary vaccines, or biological enzymes for industrial use.

The AMP program will consider a wide range of novel and non-traditional protein manufacturing platforms provided that they are capable of producing high quality monoclonal antibody and vaccines within the radically-shortened timelines. Candidate systems might include fungal fermentation, arthropod-transected systems, aquatic and terrestrial plant systems, or comparable systems derived from other applications. Each system will be given careful consideration. One key consideration is that protein production must be extremely flexible as the system will need to produce a wide range of proteins after being given the proper DNA construct. All platform systems will need to demonstrate production of a minimum of three proteins, one picked by the proposer and two test cases, where an unknown "target protein" representing a new threat agent is selected by DARPA. Manufactured proteins may be either a small vaccine antigen or a monoclonal antibody; however, **DARPA will give preference to technologies that are capable of producing the widest range of simple, complex and dimerized proteins.**

3.1 Program Milestones

The milestones and goals of this program are aggressive, and require expertise in molecular biology, protein synthesis, accelerated protein manufacture, cost modeling and certified Good Manufacturing Practices (cGMP) regulations. In order to achieve the program goal of 3 million doses in 12 weeks, AMP is divided up into three phases of escalating capability. Each phase has milestones that require logarithmic improvements in efficiency, production speed, and cost effectiveness as outlined in Table 1. As a point of clarification, "dose" refers to amount of purified protein that is considered typical for an efficacious product. For a vaccine antigen, protein quantity is approximately ~50ug, and for a monoclonal antibody (mAB) ~400mg. The program milestones for each of the three Phases are provided in the table below:

AMP Milestones

	Phase I 12 months	Phase II 15 months	Phase III 15 months
Manufacturing Rate (V= 40mcg; mAB= 400mg)	V ≥ 1 dose/ (L * wks) mAB ≥ 0.025 doses/(L * wks)	V ≥ 10 dose/ (L * wks) mAB ≥ 0.25 doses/(L * wks)	V ≥ 100 dose/ (L * wks) mAB ≥ 2.5 doses/(L* wks)
Scale Up	Demonstrate pathway to scale up	30L* in 12 wks	3 * 10^6 doses in 12 wks
Cost	Demonstrate path to Phase III Cost Goals	Demonstrate path to Phase III Cost Goals	Manufacture Costs are Vaccine ≤ $1/dose mAB ≤ $10/dose
Biochemistry			
Solubility	mAB >90%, Vaccine >90%	mAB >95%, Vaccine >95%	mAB >98%, Vaccine >98%
Fragment	mAB <10%, Vaccine <10%	mAB <1%, Vaccine <1%	mAB <.1%, Vaccine <.1%
Folding	mAB >92%, Vaccine >92%	mAB >95%, Vaccine >95%	mAB >99.9%, Vaccine >99.9%
Live Fire Test		Manufacture drug against DARPA-designated *unknown agent* in 3 months	Manufacture 3x10^6 doses against 2ND DARPA-designated *unknown agent* in 3 months

cGMP= Certified Good Manufacturing Practices * or equivalent using alternative system

Table I

Note that AMP program milestones listed under "Biochemistry" were selected to provide a correlate method for ascertaining protein manufacturing efficiency across an extraordinary range of candidate biological systems. These milestones; solubility, fragmentation and folding, are <u>not</u> to be interpreted as an accepted criteria for certified GMP protein therapeutic manufacture.

In Phase I (12 months), the proposer must demonstrate that the synthesized protein has proper structure and functionality as demonstrated by routine biophysical and biochemical assays such as chromatography and mass spectrometry. Phase I requires that the performer outline a plan to demonstrate protein purity and proper protein folding. As part of the Phase I milestones, the proposer must also demonstrate a clear plan as to how they will achieve the milestones in Phase III, including cost estimates for protein production during manufacture at larger scale.

In Phase II (15months), the required or equivalent rate of protein production increases 10-fold and should be demonstrated in standard 30L fermenters or equivalent using alternate protein manufacturing platforms, over a period of 12 weeks. Requirements for proper structure of the manufactured protein also become more stringent. Phase II includes the first of two DARPA Challenges known as "Live Fire Tests" in which the proposer has 3-months to manufacture a vaccine or monoclonal antibody against a DARPA-selected target. The Live Fire Test provides an objective measure of the proposer's technical capability.

Phase III (15 months) will achieve the overall goal of producing 3 million doses of a protein therapeutic within 12 weeks in a second DARPA Live Fire Test. Phase 3 will also require an additional 10-fold increase in the speed of manufacturing compared to Phase II. In Phase III, the estimated costs of manufacture should be less than $1/dose for a vaccine and less than $10/dose for a mAB.

Special Case: Non-fermentative Alternative Protein Manufacture

Proposers that present alternative protein manufacture such as plant-based, algal, arthropod, transgenic and other non-fermentative based protein manufacturing systems must indicate a metric for assessing equivalent measures to the yield of doses/(liters*week). For example, a proposal relying on plant-based monoclonal antibody production, which might be measured in doses per acre or Kg dry weight of biomass, must provide and defend their rate metric for each of the three phases.

3.2 Team Organization

The aggressive goals of the AMP Program require that each proposal include a multi-disciplinary team with demonstrated (or established) capability. The composition of the team might include large pharmaceutical companies, small biotechnology companies, academic research laboratories, pharmaceutical consultant groups, enzyme and alcohol manufacturers and privately funded research programs. Proposals that center solely on one research sub-component, while neglecting the overall vision and required end capability, will not be considered for funding. At a minimum, teams are expected to possess expertise or demonstrate collaboration with members in the following areas:

a) Molecular Biology- with expertise in protein cloning, purification processes and optimization of growth conditions.
b) Protein Chemistry- with expertise in structure of proteins and post-translational modification (e.g. amidation and glycosylation)
c) Manufacturing- expertise in large scale production of proteins.
d) Expertise in FDA certified Good Manufacturing Processes (c GMP) regulations

3.3 Integration Partner

Strong, competent team leadership is essential for successful implementation of the elements of this program. For this reason, it is critical that the research team be organized around a dedicated integration partner known as a Systems Integrator (SI), who has the responsibility of overall program management and who will maintain a focus on the AMP objectives. The SI will take responsibility for the accomplishment of all milestones as well as transition of the completed platform to the commercialization partner. During the course of performance, it is expected that some team members may be more active than others and that team members may need to be replaced. As such the SI must have the authority to develop and maintain the proper team membership to ensure successful on-time completion of all tasks, and within the research budget.

A successful proposal will demonstrate strong expertise and experience within the teams, understanding of the challenges, current data, access to facilities to conduct the proposed work, and most importantly, a clear plan to achieve the specific milestones of the program. It is left to

the discretion of the proposer to construct their team from the private, academic and commercial parties that will be necessary to carry out the effort.

Since team composition will ultimately determine the success of this program, a teaming website will be set up to facilitate these interactions (http://www.sainc.com/ampteaming/)

4.0 General Information

Proposals not meeting the format described in this pamphlet may not be reviewed. Proposals MUST NOT be submitted by fax; any so sent will not be accepted. This notice, in conjunction with the BAA06-31, FedBizOpps Announcement, and all references, constitutes the entire announcement. If there is any conflict between this PIP and the published BAA, the BAA takes precedence.

Other supporting or background materials submitted with the white paper or full proposal will be considered for the reviewer's convenience only and not considered as part of the white paper or proposal.. White papers and proposals received by fax will not be accepted.

No additional information is available, nor will a formal Request for Proposal (RFP) or other solicitation regarding this announcement be issued. Requests for same will be disregarded.

All responsible sources capable of satisfying the Government's needs may submit a proposal that shall be considered by DARPA. Small Disadvantaged Businesses (SDB), Historically Black Colleges and Universities (HBCUs) and Minority Institutions (MIs) are encouraged to submit proposals and join others in submitting proposals. However, no portion of this BAA will be set aside for SDB, HBCU and MI participation due to the impracticality of reserving discrete or severable areas of this research for exclusive competition among these entities.

5.0 Submission Process

WHITE PAPERS

DARPA encourages the submission of White Papers to allow for comments to the proposer.

White papers sent in response to BAA06-31 are due at DARPA no later than 1600 ET, May 17, 2006.

White papers should be concise and limited to 8 pages in length. The white paper must be organized as follows:

1. An Executive Summary. A one page statement of the uniqueness of the idea. The AMP program is looking for systems that will generate revolutionary capabilities in protein drug production at the conclusion of the 42-month project.
2. A concise statement of the scientific and technical challenges, and anticipated solutions to the challenges that will be addressed. This statement should demonstrate that the proposer has a

clear understanding of current protein manufacturing systems, including shortcomings in current capability.
3. A response to the milestones set forth for Phase I and Phase II as well as a discussion of path to accomplish the milestones in Phase III. Milestones must reflect a period of performance of 12 months for Phase I and 15 months each for both Phase II and III (please note details regarding the 3-month Live Fire Tests). Milestones must be associated with demonstrable metrics of performance.
4. A cost estimation for resources required for Phase I and Phase II. This should include a clear description of subcontracted services, human resources and distribution of expenditures over calendar, academic or fiscal years.
5. A brief summary of the technical expertise of the System Integrator and other key research members, and a management plan for multi-organizational teams.
6. Brief list of relevant references.

To facilitate the submission of white papers, a website has been established,
http://www.sainc.com/dso0631/dsowhitepaper/index.asp

Within two weeks of receipt of the white paper, the proposer will receive a confirmation providing a log number. The formal recommendation about whether a full proposal is recommended will be made as soon as possible. However, the exact time for response will depend on a variety of circumstances, including the number of white papers received. Please note: Feedback provided is for the benefit of the proposer and following these recommendations is not a guarantee that the full proposal will be funded.

Not withstanding the disposition of white papers, DARPA will accept full proposals for BAA.

FULL PROPOSALS:
White Papers will be accepted for this BAA. The process and contents of the White Papers are discussed above.

Proposals may be submitted and received at any time until the final proposal deadline of 1600 ET June 21, 2006.

Proposals will be evaluated against the criteria set forth in Section 7 of this PIP, and a proposer will be notified either that: 1) the proposal has been selected for funding, or 2) the proposal has not been selected for funding. Proposers may elect to have their proposal withdrawn from consideration at any time during the evaluation process. If a formal request is not made, DARPA will assume that continued evaluation is desired. Proposals not conforming to the instructions provided in the BAA and PIP may not be evaluated at the discretion of the Government.

To facilitate the submission of full proposals, a website has been established,
http://www.sainc.com/dso0631/dsofullproposal/index.asp

This site will allow the filling in of contact information and the uploading of a full proposal created with the requirements listed below and the uploading of a document in either Word or PDF format. Note: if the website is not used, please use the U.S. mail system or the BAA e-mail

account. If submitting via e-mail, the body of the e-mail AND the attachment must include name, mailing address, phone number, and fax of the proposer. If this information is not contained in the body, the e-mail will be returned for inclusion of that information. If proposers choose to submit by U.S. Mail, they should submit one (1) original and three (3) copies of the full proposal to

DARPA/DSO, ATTN: **BAA06-31**
3701 North Fairfax Drive
Arlington, VA 22203-1714.

Proposals **will not** be accepted by way of facsimile transmissions.

6.0 Proposal Format

Format and content of full proposals: The descriptions contained in this section are to help proposers ensure that proposals have sufficiently detailed information to be evaluated. Full proposals shall consist of two volumes, technical and cost. Both volumes should be included as a single document when uploading to the website.

6.1 Volume I: Technical

This volume provides the detailed discussion of the proposed work necessary to enable an in-depth review of the specific technical and management issues. Specific attention must be given to addressing both the risk and payoff of the proposed work that make it desirable to DARPA. While it is expected that the technical details of the Phase I effort will be more fully discussed, the proposal must cover Phase I, Phase II and discussion of pathway to Phase III.

The Technical Volume shall not exceed 30 pages (not including Research Involving Human Use which will not be included in the total number of pages but should remain as concise as possible), including a one page concise summary, (one-inch margins and size 12 Times New Roman font) and shall address sections A through L. While proposers are free to decide the emphasis given to each section, the suggested page lengths for each section are shown in braces { } below, where applicable.

A. Summary -Innovative claims for the proposed research {1 Page}. This page is the centerpiece of the proposal and should succinctly describe the unique proposed contribution.

B. Proposal Roadmap {2 Pages}. The roadmap provides a top-level view of the content and structure of the proposal. It contains a synopsis (or "sound bite") for each of the eight areas defined below. It is important to make the synopses as explicit and informative as possible. The roadmap must also cross-reference the proposal page number(s) where each area is elaborated. The eight roadmap areas are:

1. Main goals of the proposed research.
2. Critical technical barriers (i.e., technical limitations that have, in the past, prevented achieving the proposed results).

3. Main elements of the proposed approach and quantification of expected results.
4. Rationale that builds confidence that the proposed approach will overcome the technical challenges listed in *Section 3.1* (Program Milestones)
5. Specific capabilities of systems integrator (documentation of previous experience and accomplishments with diverse, multidisciplinary efforts).
6. Uniqueness of capabilities or approach. Platforms that are diversified from the norm, yet proven to be efficacious such as plant, fungus, arthropod, etc will be given special consideration
7. Criteria for scientifically evaluating progress and capabilities on a quarterly basis.
8. Cost of the proposed effort for each performance year.

C. Statement of Work {2 Pages}. Detailed statement of work, written in plain English, outlining the scope of the effort and citing specific tasks to be performed, references to specific subcontractors, if applicable, and specific contractor requirements.

D. Research Objectives {1 Page}

1. Strategic Description. Provide concise description of strategies used to address problematic area in this research project.
2. Research Goals. Identify specific research goals of this project. Identify and quantify expected performance outcomes from this research with respect to metrics described here and in the BAA. Describe new capabilities enabled by this research and how such advances address program goals.

E. Technical Approach:

1. Detailed Description of Technical Approach {10 Pages}. Provide detailed description of technical approach(es) that will be used in this project to achieve research goals. Specifically identify and discuss how advances will be incorporated into the final product.
2. Comparison with Current Technology {2 Pages}. Describe state-of-the-art approaches and the limitations within the context of the problem area addressed by this research. Proposers must state explicitly how they will improve upon state of the art research.

F. Schedule and Milestones

1. Schedule Graphic {2 Pages}. Provide a graphic representation of project schedule including detail down to the individual effort level. This should include, but not be limited to, a multi-phase development plan that demonstrates a clear understanding of the proposed research. Show all project milestones. Use absolute designations for all dates. In this section, font may be decreased to size 8 Times New Roman.
2. Detailed Individual Effort Descriptions {2 Pages}. Provide detailed task descriptions for each individual effort and/or subcontractor in schedule graphic.

G. *Deliverables Description* {2 Pages} List and provide detailed description for each proposed deliverable. Include in this section all proprietary claims to results, platforms, or systems

supporting and/or necessary for the use of the research, results, and/or platform. If there are no proprietary claims, this should be stated. The proposer must submit a separate list of all technical data or computer software that will be furnished to the Government with other than unlimited rights (see DFARS 227). Specify receiving organization and expected delivery date for each deliverable.

H. Technology Transition and Technology Transfer Targets and Plans {2 Page}. Discuss path for technology transition and transfer to Phase III of the program. Proposers should also provide a plan for transition of appropriate technology components and information to the user community. The role of the SI in this transition must be explicitly described.

I. Personnel and Qualifications {2 Pages}. List of key personnel, concise summary of their qualifications, and discussion of proposer's previous accomplishments and work in this or closely related research areas. Proposers must indicate the level of effort to be expended by each person during each contract year and identify other (current and proposed) major sources of support for them and/or commitments of their efforts. DARPA expects all key personnel associated with a proposal to make a substantial time commitment to the proposed activity. The Principal Investigator (PI) must be included as a key person and must be a full-time employee of the organizing facility.

J. Facilities {2 Pages}. Description of the facilities that would be used for the proposed effort. Since this is expected to be a multi-team effort, the proposal should make clear which facilities will be used for which portion of the effort. If any portion of the research is predicated upon the use of Government Owned Resources of any type, the proposer shall specifically identify the property or other resource required, the date the property or resource is required, the duration of the requirement, the source from which the resource is required, if known, and the impact on the research if the resource cannot be provided. If no Government Furnished Property is required for conduct of the proposed research, the proposal shall so state.

K. Research Involving Human Use {This does not factor into the total number of pages but should be as concise as possible): Proposals selected for funding are required to comply with provisions of the Common Rule (32 CFR 219) on the protection of human subjects in research (http://www.dtic.mil/biosys/downloads/32cfr219.pdf) and the DoD Directive 3216.2 (http://www.dtic.mil/whs/directives/corres/html2/d32162x.htm). All proposals that involve the use of human subjects are required to include documentation of their ability to follow Federal guidelines for the protection of human subjects. This includes, but is not limited to, protocol approval mechanisms, approved Institutional Review Boards (IRB), and Federal Wide Assurances. These requirements are based on expected human use issues sometime during the entire length of the proposed effort.

For proposals involving "greater than minimal risk" to human subjects within the first year of the project, performers must provide evidence of protocol submission to a Federally approved IRB at the time of final proposal submission to DARPA. For proposals that are forecasted to involve "greater than minimal risk" after the first year, a discussion on how and when the proposer will comply with submission to a Federally approved IRB needs to be provided in the submission. More information on applicable Federal regulations can be found at the Department of Health

and Human Services Office of Human Research Protections website (http://www.dhhs.gov/ohrp/).

L. Patent Information (This does not factor into the total number of pages but should be as concise as possible): Please include documentation proving your ownership of or possession of appropriate licensing rights to all patented inventions (or inventions for which a patent application has been filed) that will be utilized under your proposal for the DARPA program. If a patent application has been filed for an invention that your proposal utilizes, but the application has not yet been made publicly available and contains proprietary information, you may provide only the patent number, inventor name(s), assignee names (if any), filing date, filing date of any related provisional application, and a summary of the patent title, together with either: 1) a representation that you own the invention, or 2) proof of possession of appropriate licensing rights in the invention. Please also provide a good faith representation that you either own or possess appropriate licensing rights to all other intellectual property that will be utilized under your proposal for the DARPA program. If you are unable to make such a representation concerning non-patent related intellectual property, please provide a listing of the intellectual property to which you do not have needed rights, and provide a detailed explanation concerning how and when you plan to obtain these rights.

6.2 Volume 2: Cost

The cost volume shall begin with a single cover page that includes the following:

1. BAA number
2. Technical area
3. Lead organization submitting proposal
4. Type of business (Lead organization), selected among the following categories: LARGE BUSINESS, SMALL BUSINESS, SMALL DISADVANTAGED BUSINESS, 8A, OTHER SMALL BUSINESS, EMERGING SMALL BUSINESS, VETERAN-OWNED SMALL BUSINESS, SERVICE-DISABLED VETERAN OWNED, OTHER VETERAN, WOMAN-OWNED BUSINESS, HUBZONE, JWOD PARTICIPATING NONPROFIT AGENCY, OTHER NONPROFIT, HOSPITAL, FOREIGN CONCERN OR ENTITY, DOMESTIC FIRM PERFORMING OUTSIDE U.S., HISTORICALLY BLACK COLLEGE OR UNIVERSITY (HBCU), MINORITY INSTITUTION (MI), OTHER EDUCATIONAL
5. Contractors reference number (if any)
6. Other team members (if applicable) and type of business for each (please use business types from Section 5.2.4)
7. Proposal title
8. Technical point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), electronic mail (if available)
9. Administrative point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), and electronic mail (if available)
10. Award instrument requested: cost-plus-fixed-fee (CPFF); cost-contract--no fee; cost sharing contract--no fee; or other type of procurement contract (specify), grant, cooperative agreement, or other transaction
11. Place(s) and period(s) of performance
12. Total proposed cost separated by basic award and option(s) (if any)

13. Name, address, and telephone number of the proposer cognizant Defense Contract Management Agency (DCMA) administration office or Office of Naval Research
14. Name, address, and telephone number of the proposers cognizant Defense Contract Audit Agency (DCAA) audit office
15. Date proposal was prepared
16. DUNS, TIN, CAGE CODE; and
17. All subcontractors proposal backup documentation to include items 1-16 above, as applicable and available.

All proprietary information should be marked on the full proposal. It is the policy of DARPA to treat all proposals as competitive information and to disclose their contents only for the purpose of evaluation. Standard proprietary disclaimers notwithstanding, proposals may be reviewed by non-Government technical experts who have signed a nondisclosure agreement with DARPA, unless the specific phrase TO BE REVIEWED BY GOVERNMENT EMPLOYEES ONLY appears on the cover sheet. In any case, personnel under exclusive contract with DARPA who have completed the appropriate nondisclosure agreements will handle the proposals for administrative purposes

Cost proposals are not subject to page limits, total program cost broken down by major cost items (direct labor, subcontracts, materials, travel, other direct costs, overhead charges, etc.), and an itemization of major subcontracts (labor, travel, materials and other direct costs) and equipment purchases. Where the effort consists of multiple portions that could reasonably be partitioned for purposes of funding, these should be identified as options with separate cost estimates for each. Supporting cost and pricing information in sufficient detail to substantiate the summary cost estimates in above. Include a description of the method used to estimate costs and supporting documentation.

Proposers should expect to participate in teams and workshops to provide specific technical background information to DARPA, attend semi-annual PI meetings, and participate in numerous other coordination meetings via teleconference or Video Teleconference (VTC). Funding to support these various group experimentation efforts should be included in technology project bids.

Note: cost or pricing data as defined in the Federal Acquisition Regulation (FAR) Subpart 2.101 shall be required if the proposal is for a procurement contract award of $550,000 or greater unless the proposer requests an exception from the requirement to submit cost or pricing data. Cost or pricing data is not required if the proposer proposes an award instrument other than a procurement contract (e.g., a grant, cooperative agreement, or other transaction). The requirements for submission of cost or pricing data are specified in FAR Subpart 15.403-4 (see http://www.arnet.gov/far).

Guidance for Classified Information and Data

The Government anticipates that proposals submitted under a BAA will be unclassified.

In the event that a proposer chooses to submit a classified proposal, the following information is applicable.

Proposals may contain classified information or data (up to the level of Top Secret/SCI). HOWEVER, DO NOT SEND CLASSIFIED FULL PROPOSALS BY EMAIL OR VIA ONLINE SUBMISSION SYSTEMS.

Proposers that intend to include classified information or data in their proposals should contact DARPA security at (571) 218-4842 (or alternatively, the point-of-contact for this BAA) for security guidance and direction in advance of proposal preparation. Proposers must have existing approved capabilities (personnel and facilities) to perform research and development at the classification level they propose.

Security Classification guidance on DD Form 254 will not be provided at this time since DARPA is soliciting ideas only. After reviewing the incoming proposals, if a determination is made that the award instrument may result in access to classified information, a DD Form 254 will be issued and attached as part of the award.

Proposers choosing to submit a classified proposal must first receive permission from the Original Classification Authority to use their information in applying to this BAA. An applicable classification guide should be submitted to ensure that the proposal is protected appropriately.

For instructions on submitting Classified Full Proposals, contact Security & Intelligence Directorate (SID) Classification Management at (571) 218-4842.

6.3 Organizational Conflict of Interest

Awards made under this BAA may be subject to the provisions of the Federal Acquisition Regulation (FAR) Subpart 9.5, Organizational Conflict of Interest. All proposers and proposed subcontractors must affirmatively state whether they are supporting any DARPA technical office(s) through an active contract or subcontract. All affirmations must state which office(s) the proposer supports, and identify the prime contract number. Affirmations should be furnished at the time of proposal submission. All facts relevant to the existence or potential existence of organizational conflicts of interest, as that term is defined in FAR 2.101, must be disclosed in the proposal, organized by task and year. This disclosure shall include a description of the action the contractor has taken, or proposes to take, to avoid, neutralize, or mitigate such conflict.

7.0 Evaluation and Funding Information

Proposals will not be evaluated against each other, since they are not submitted in accordance with a common work statement. DARPA's intent is to review proposals as soon as possible after they arrive. For evaluation purposes, a proposal is the document described in Proposal Format. Other supporting or background materials submitted with the proposal will be considered for the reviewer's convenience only and not considered as part of the proposal. DARPA reserves the right to request an oral presentation of proposals. If such a request is made, it is expected that, to the extent possible, all key personnel on the team will be present. The request for an oral

presentation, or lack thereof, should not be construed as either a positive or negative assessment of the proposal.

The following evaluation criteria are listed in order of decreasing importance. Proposals that are deemed unsatisfactory in Scientific and Technical merit will not be evaluated further.

Scientific and Technical Merit

Proposals will be evaluated as follows: Proposers must demonstrate that their proposal is innovative and unique, that the technical approach is sound, that they have an understanding of critical technical issues and risk and that they have a plan for mitigation of those risks. A significant improvement in capability or understanding above the state of the art in the manufacture of biological pharmaceuticals must be demonstrated. A key consideration is that protein production be extremely flexible as the system will need to produce a wide range of proteins after being given the proper DNA construct. A critical part of the evaluation is to provide details describing a clear pathway to a Phase III transition including plans for transition to a commercialization partner capable of producing protein therapeutics that are eligible for FDA approval. All milestones must be clearly and quantitatively described. Proposers are encouraged to avoid obscure language and indeterminate measures of success as these will not help the application.

Value to Defense

Proposals will be evaluated as follows: Proposers must demonstrate the AMP vision to create technologies that will enable the Department of Defense to have a rapid (within weeks) and highly effective medical therapeutic response to any intentional or naturally emergent pathogen.

Capability of the Personnel and Facilities to Perform the Proposed Effort

Proposals will be evaluated as follows: Proposers must demonstrate that their team has the necessary background and experience to perform this project. Interdisciplinary team should include expertise or demonstrated collaboration in molecular biology, protein chemistry, and manufacturing expertise in FDA certified cGMP regulation. Systems integrator (SI) is responsible for ensuring that the team meets all milestones and metrics and integration of all proposed research. Facilities should be detailed with discussion of any unique capabilities pertinent to the research. Expertise can be acquired from many sources including consultant groups with an active stake in the program.

Cost Realism

Proposals will be evaluated as follows:
The objective of this criterion is to assure that proposed cost is consistent with proposed effort.
The proposed cost will be evaluated as follows:
Proposals will be evaluated as follows: Costs are justified in relation to the scope of the proposed program. Other funding sources and activities are taken into account. A budget for an optional second and third phase is provided and includes justification of all costs.

The Government reserves the right to select all, some, or none of the proposals received in response to this solicitation and to make awards without discussions with proposers; however, the Government reserves the right to conduct discussions if the Source Selection Authority later

determines them to be necessary. Proposals identified for funding may result in a contract, grant, cooperative agreement, or other transaction depending upon the nature of the work proposed, the required degree of interaction between parties, and other factors. If warranted, portions of resulting awards may be segregated into pre-priced options.

8.0 Administrative Addresses

Web address for White Paper Submission:
http://www.sainc.com/dso0631/dsowhitepaper/index.asp

Web address for Full Proposal Submission:
http://www.sainc.com/dso0631/dsofullproposal/index.asp

DARPA/DSO, ATTN: **BAA06-31**
3701 North Fairfax Drive
Arlington, VA 22203-1714

Electronic Mail: BAA06-31@darpa.mil

Related URLs:
BAA 06-31: http://www.darpa.mil/baa/baa06-31.html
PIP 06-31: http://www.darpa.mil/dso/solicitations/AMPPIP.pdf
Teaming Website BAA 06-31: http://www.sainc.com/ampteaming/

Point of Contact:
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Program Manager, DSO
Phone (571) 218-4596
Email: Michael.Callahan@darpa.mil
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